

Attached to #10

Substitute for PTO/SB/8A (Modified) INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary)		Complete if Known	
		Application Number	09/990,433
		Filing Date	November 20, 2001
		First Named Inventor	ZARLING, David A.
		Group Art Unit	1633-1636
		Examiner Name	KAUSHAL
Sheet 1 of 8	Attorney Docket Number	A-64580-5/RFT/NBC (467135-38)	

U.S. PATENT DOCUMENTS					
Examiner Initials*	Cite No.	U.S. Patent Document Number-Kind Code ² (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
Se	A1	4,873,191	10/1989	Wagner et al.	
Se	A2	4,888,274	12/1989	Radding et al.	
Si	A3	4,950,599	08/1990	Bertling	
Se	A4	5,223,414	06/1993	Zarling et al.	
Se	A5	5,264,618	11/1993	Felgner et al.	
Se	A6	5,272,071	12/1993	Chappel	
Se	A7	5,273,881	12/1993	Sena et al.	
Se	A8	5,366,894	11/1994	Clark et al.	
Se	A9	5,416,260	05/1995	Koller et al.	
Se	A10	5,451,513	09/1995	Maliga et al.	
Se	A11	5,459,072	10/1995	McKay et al.	
Se	A12	5,460,941	10/1995	Camerini-Otero et al.	
Se	A13	5,464,764	11/1995	Capecchi et al.	
Se	A14	5,468,629	11/1995	Calhoun	
Se	A15	5,487,992	01/1996	Capecchi et al.	
Se	A16	5,501,967	03/1996	Offringa et al.	
Se	A17	5,506,098	04/1996	Zarling et al.	
Se	A18	5,510,473	04/1996	Camerini-Otero et al.	
Se	A19	5,527,674	06/1996	Guerra et al.	
Se	A20	5,543,131	08/1996	Levy	
Se	A21	5,545,806	08/1996	Lonberg et al.	
Se	A22	5,565,350	10/1996	Kmiec	
Se	A23	5,571,688	11/1996	Mekalanos et al.	
Se	A24	5,578,461	11/1996	Sherwin et al.	
Se	A25	5,580,734	12/1996	Treco et al.	
Se	A26	5,589,369	12/1996	Seidman et al.	

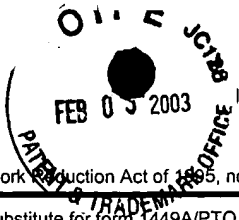
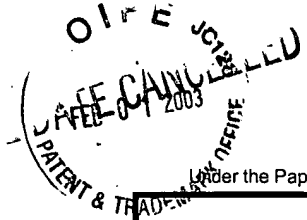
RECEIVED
FEB 05 2003
TECH CENTER 1600/2900

Examiner Signature		Date Considered	10/6/03
--------------------	--	-----------------	---------

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Unique citation designation number. ² See attached Kinds of U.S. Patent Documents at www.uspto.gov or MPEP 901.04. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶ Applicant is to place a check mark here if English Language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231. 1102232_1.DOC



Substitute PTO/SB/8A (08-00)

Approved for use through 10/31/2002. OMB 0651-0031

U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary)				Complete if Known	
				Application Number	09/990,433
				Filing Date	November 20, 2001
				First Named Inventor	ZARLING, David A.
				Group Art Unit	4633-1636
				Examiner Name	KAUSHAL
Sheet	2	of	8	Attorney Docket Number	A-64580-5/RFT/NBC (467135-38)

U.S. PATENT DOCUMENTS

Examiner Initials*	Cite No.	U.S. Patent Document Number-Kind Code ² (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
2	A27	5,612,205	03/1997	Kay et al.	
2	A28	5,614,396	03/1997	Bradley et al.	
8	A29	5,763,240	06/1998	Zarling et al.	
8	A30	5,948,653	09/1999	Pati et al.	
8	A31	6,255,113 B1	07/2001	Zarling et al.	
8	A32				

FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No.	Foreign Patent Document Country Code ² Number ⁴ Kind Code ⁵ (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T ⁶
8	B1	EP 0 718 404	11/1995	TAKARA SHUZO CO. (JP)		
8	B2	WO 91/19796	12/1991	BAYLOR COLLEGE MED (US)		
8	B3	WO 92/08791	05/1992	US COMMERCE (US)		
8	B4	WO 92/15694	09/1992	SALK INST BIOLOG STUD (US)		
8	B5	WO 93/03736	03/1993	MICROPROBE CORP (US)		
8	B6	WO 93/05177	03/1993	DAIKIN IND LTD (JP)		
8	B7	WO 93/05178	03/1993	DAIKIN IND LTD (JP)		
8	B8	WO 93/22443	11/1993	STANFORD RES INST INT (US)		
8	B9	WO 94/04032	03/1994	UNIV CALIF (US)		
8	B10	WO 94/04669	03/1994	MEDICAL RES COUNSEL (GB)		
8	B11	WO 95/22625	08/1995	AFFYMAX TECH NV (AN)		
8	B12	WO 96/03051	02/1996	GENE PHARMING EUROP (NL)		
8	B13	WO 96/40765	12/1996	U.S. DEPT HEALTH (US)		
8	B14	WO 97/04111	02/1997	U.S. DEPT HEALTH (US)		
8	B15	WO 97/05268	02/1997	SETRATECH (FR)		
8	B16					
8	B17					
8	B18					

RECEIVED
FEB 05 2003
TECH CENTER 1600/2900

Examiner Signature		Date Considered	12/6/03
--------------------	--	-----------------	---------

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Unique citation designation number. ² See attached Kinds of U.S. Patent Documents at www.uspto.gov or MPEP 901.04. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶ Applicant is to place a check mark here if English Language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231. 1102232_1.DOC

OIPE
 FEB 0 1 2003
 PATENT & TRADEMARK OFFICE
 RECEIVED
 FEB 0 1 2003

Substitute PTO/SB/8A (08-00)
 Approved for use through 10/31/2002. OMB 0651-0031
 U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE
 Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449A/PTO (Modified)			Complete if Known		
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary)			Application Number	09/990,433	
			Filing Date	November 20, 2001	
			First Named Inventor	ZARLING, David A.	
			Group Art Unit	1633-1676	
			Examiner Name	KAVSHAN	
Sheet	3	of	8	Attorney Docket Number	A-64580-5/RFT/NBC (467135-38)

RECEIVED

FEB 05 2003

TECH CENTER 1600/2900

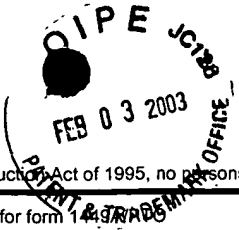
OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS					
Examiner Initials*	Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.			
✓	C1	AFONINA, I., et al., "Sequence-specific arrest of primer extension on single-stranded DNA by an oligonucleotide-minor groove binder conjugate", Proc. Natl. Acad. Sci. USA, 93:3199-3204 (Apr. 1996).			
✓	C2	ANDERSON, W.F., "Human gene therapy." Nature. 1998 Apr 30;392(6679 Suppl):25-30.			
✓	C3	AUSUBEL et al., "Short Protocols in Molecular Biology," 2nd ed. (John Wiley & Sons: New York), pp. 9-14 and 9-15 (1992).			
✓	C4	BERTLING, "Transfection of a DNA/Protein Complex into Nuclei of Mammalian Cells Using Polyoma Capsids and Electroporation," Bioscience Reports, 7:107-111 (1987).			
✓	C5	BERTOLOTTI, R., "Recombinase-mediated Gene Therapy", Bionews, Newsletter of BioTechnology, Health and Environmental Sciences, N14 (Nov. 1996).			
✓	C6	BRADLEY, A. et al., "Modifying the mouse: design and desire." Biotechnology (N Y). 1992 May;10(5):534-9			
✓	C7	CAMERINI-OTERO, R.D., et al., "Homologous Recombination Proteins in Prokaryotes and Eukaryotes", Annu. Rev. Genetics, 29:509-52 (1995).			
✓	C8	CASSUTO, et al., "Initiation of genetic recombination" Homologous pairing between duplex DNA molecules promoted by recA protein," Proc. Natl. Acad. Sci. USA, 77(7):3962-3966 (1980).			
✓	C9	CHENG et al., "RecA-Directed Hybridization of Psoralen-Monoadducted DNA Oligonucleotides to Duplex Targets," NATO ASI Ser., Ser C., Photochemical Probes in Biochemistry, 272:169-177, P.E. Nielsen (ed.), (1989).			
✓	C10	CLARKE et al., "Defective Epithelial Chloride Transport in a Gene-Targeted Mouse Model of Cystic Fibrosis," Science, 257:1125-1128 (1992).			
✓	C11	CLERMONT, Y. et al., "Structure of the Golgi Apparatus in Stimulated and Nonstimulated Acinar Cells of Mammary Glands of the Rat," The Anatomical Record 237:308-317 (1993).			
✓	C12	CLERMONT, et al., "Transport of Casein Submicelles and Formation of Secretion Granules in the Golgi Apparatus of Epithelial Cells of the Lactating Mammary Gland of the Rat," The Anatomical Record 235:363-373 (1993).			
✓	C13	COLE-STAUS, A., et al., "Correction of the Mutation Responsible for Sickle Cell Anemia by an RNA-DNA Oligonucleotide", Science, Vol.273:1386-1389 (Sep. 1996).			
✓	C14	COX et al., "Enzymes of General Recombination," Ann. Rev. Biochem, 56:229-262 (1987).			
✓	C15	CRAMERI, A., et al., "Improved Green Fluorescent Protein by Molecular Evolution Using DNA Shuffling", Nature BioTech., 14:315-319 (Mar. 1996).			
✓	C16	CRAMERI, A., et al., "Construction and evolution of antibody-phage libraries by DNA shuffling", Nature Medicine, Vol.2, No.1:100-102 (Jan. 1996).			
✓	C17	DECHIARA, T.M. et al., "A growth-deficiency phenotype in heterozygous mice carrying an insulin-like growth factor II gene disrupted by targeting." Nature. 1990 May 3;345(6270):78-80			

Examiner Signature	<i>[Signature]</i>	Date Considered	10/6/03
--------------------	--------------------	-----------------	---------

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Unique citation designation number. ² See attached Kinds of U.S. Patent Documents at www.uspto.gov or MPEP 901.04. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶ Applicant is to place a check mark here if English Language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231. 1102232_1.DOC



Substitute PTO/SB/8A (08-00)

Approved for use through 10/31/2002. OMB 0651-0031
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449 (Modified)		Complete if Known	
		Application Number	09/990,433
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary)		Filing Date	November 20, 2001
		First Named Inventor	ZARLING, David A.
		Group Art Unit	1633 1636
		Examiner Name	K A USHOL
		Attorney Docket Number	A-64580-5/RFT/NBC (46135-38)
Sheet	4	of	8

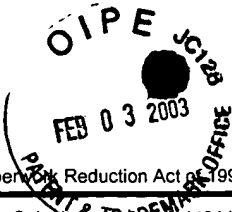
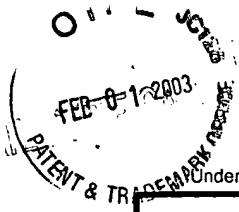
RECEIVED
FEB 05 2003
TECH CENTER 1600/2900

OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	†
C	C18	DRUMM, et al., "Correction of the Cystic Fibrosis Defect In Vitro by Retrovirus-Mediated Gene Transfer," Cell, 62:1227-1233 (1990).	
D	C19	DUNDERDALE, et al., "Formation and Resolution of Recombination Intermediates by E. Coli RecA and RuvC Proteins," Nature, 354(19):506-510 (1991).	
C	C20	FABRE, J.W. "Nudging xenotransplantation towards humans." Nat Med. 1995 May;1(5):403-4.	
D	C21	FELGNER et al. "Lipofection: A Highly Efficient, Lipid-Mediated DNA-Transfection Procedure," Proc. Natl. Acad. Sci. USA, 84:7413-7417 (1987).	
C	C22	FIELDS and JANG, "Presence of a Potent Transcription Activating Sequence in the p53 Protein," Science, 249:1046-1049 (1990).	
C	C23	FU, D., et al., "Sequencing double-stranded DNA by strand displacement", Nucleic Acids Res., 25(3):677-679 (1997).	
C	C24	GATES, C.M., et al., "Affinity Selective Isolation of Ligands from Peptide Libraries Through Display on a lac Repressor "Headpiece Dimer"", J. Mol. Biol., 255:373-386 (1996).	
C	C25	GURDON, "The Birth of Cloning," The Sciences 26-31 (September-October 1997).	
C	C26	HAMMER, R.E. et al., "Spontaneous inflammatory disease in transgenic rats expressing HLA-B27 and human beta 2m: an animal model of HLA-B27-associated human disorders." Cell. 1990 Nov 30;63(5):1099-112	
C	C27	HART, et al., "Born Again?", The Sciences 47-51 (September-October 1997).	
C	C28	HASTY et al., "Introduction of a Subtle Mutation into the Hox-2.6 Locus in Embryonic Stem Cells," Nature, 350:243-246 (1991).	
C	C29	HERZING, L.B.K., et al., "Novel lacZ-based recombination vectors for mammalian cells", Gene, 137:163-169 (1993).	
C	C30	HUNGER-BERTLING, K., et al., "Short DNA fragments induce site specific recombination in mammalian cells", Mol. and Cellular Biochem., 92:107-116 (1990).	
C	C31	HUYNH, et al., "Establishment of Bovine Mammary Epithelial Cells (MAC-T): An in Vitro Model for Bovine Lactation," Experimental Cell Research 197:191-199 (1991).	
C	C32	JASIN, M., et al., "Targeted transgenesis", Proc. Natl. Acad. Sci. USA, 93:8804-8808 (Aug. 1996).	
C	C33	JAYASENA, V.K., et al., "Complement-stabilized D-loop--RecA-catalyzed Stable Pairing of Linear DNA Molecules at Internal Sites", J. Mol. Biol., 230:1015-1024 (1993).	
C	C34	KARATZAS, et al., "Toward Altering Milk Composition by Genetic Manipulation: Current Status and Challenges," J. Dairy Sci. 80:2225-2232 (1997).	
C	C35	KEEFER, et al., "Bovine Inner Cell Mass Cells as Donor Nuclei in the Production of Nuclear Transfer Embryos and Calves," Biology of Reproduction, 50:935-939 (1994).	
Examiner Signature			Date Considered 10/6/03

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Unique citation designation number. ² See attached Kinds of U.S. Patent Documents at www.uspto.gov or MPEP 901.04. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶ Applicant is to place a check mark here if English Language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231. 1102232_1.DOC



Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute PTO/SB/8A (08-00) (Modified)		Complete if Known			
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary)		Application Number	09/990,433		
		Filing Date	November 20, 2001		
		First Named Inventor	ZARLING, David A.		
		Group Art Unit	1633 1636		
		Examiner Name	KAUSHA L		
Sheet	5	of	8	Attorney Docket Number	A-64580-5/RFT/NBC (467135-38)

RECEIVED
FEB 0 5 2003
TECH CENTER 1600/2900

OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS		
Examiner Initials*	Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.
SL	C36	KEEFER, et al., "Isolation and Maintenance of Putative Embryonic Stem (ES) Cells Derived from Nigerian Dwarf Goat Embryos," Biol. Reprod. 54(51):172 [No. 462] (1996).
SL	C37	KIDO, M., et al., "Escherichia coli RecA Protein Modified with a Nuclear Location Signal Binds to Chromosomes in Living Mammalian Cells", Exper. Cell Res., 198:107-114 (1992).
SL	C38	KONFORTI, et al., "DNA substrate requirements for stable joint molecule formation by the recA and single-stranded DNA-binding proteins of Escherichia coli," The Journal of Biological Chemistry, 266(16):10112-10121 (1991).
SL	C39	KOWALCZYKOWSKI, S.C., et al., "Homologous Recombination Proteins and their Potential Applications in Gene Targeting Technology," Gene Targeting, CRC Press: Boca Raton, ed. Manuel A. Vega, Chap. 7:167-210 (1995).
SL	C40	KUEHN, M.R. et al., "A potential animal model for Lesch-Nyhan syndrome through introduction of HPRT mutations into mice." Nature. 1987 Mar 19-25;326(6110):295-8
SL	C41	KUHN, R., et al. "Inducible gene targeting in mice." Science. 1995 Sep 8;269(5229):1427-9
SL	C42	KUNZELMANN, K., et al., "Gene targeting of CFTR DNA in CF epithelial cells", Gene Therapy, 3:859-867 (1996).
SL	C43	KUTYAVIN, I.V., et al., "Oligonucleotides Containing 2-Amino adenine and 2-Thiothymine Act as Selectively Binding Complementary Agents", Biochemistry, 35:11170-11176 (1996).
SL	C44	LANGER et al., "Enzymatic Synthesis of Biotin-Labeled Polynucleotides: Novel Nucleic Acid Affinity Probes," Proc. Natl. Acad. Sci. USA, 78(11):6633-6637 (1981).
SL	C45	LIN, Y. et al., "Morphologic Observation of Neutrophil Diapedesis Across Bovine Mammary Gland Epithelium in Vitro," Am. J. Vet. Res. 56(2):203-207 (1995).
SL	C46	LIN, et al., "Quantification of Bovine Neutrophil Migration Across Mammary Epithelium in vitro," Can. J. Vet. Res. 60:145-149 (1996).
SL	C47	LUDWIG, D.L., et al., "Spontaneous and Induced Homologous Recombination Between lacZ Chromosomal Direct Repeats in CV-1 Cells", Somatic Cell and Molecular Genetics, 20(1):11-25 (1994).
SL	C48	LUKHTANOV, E.A. et al., "Rapid and Efficient Hybridization-Triggered Crosslinking within a DNA Duplex by an Oligodeoxyribonucleotide Bearing a Conjugated Cyclopropapyrroloindole," Nucleic Acids Research, 24(4):683-687 (1996).
SL	C49	MACDONALD, et al., "Neutrophil Function In Vitro: Diapedesis and Phagocytosis," J Dairy Sci., 77:628-638 (1994).
SL	C50	MATSUMURA, I., et al., "DNA Shuffling brightens prospects for GFP", Nature BioTech., Vol. 14:366 (Mar. 1996).
SL	C51	MEADE, H. "Dairy Gene," The Sciences, 20-25 (September/October 1997).
SL	C52	MEYER Jr., R.B., et al., "Efficient, Specific Cross-Linking and Cleavage of DNA by Stable, Synthetic Complementary Oligodeoxynucleotides", J. of the Amer. Chem. Soc., 111(22):8517-8519 (1989).

Examiner Signature		Date Considered	10/6/03
--------------------	--	-----------------	---------

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Unique citation designation number. ² See attached Kinds of U.S. Patent Documents at www.uspto.gov or MPEP 901.04. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶ Applicant is to place a check mark here if English Language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231. 1102232_1.DOC

O I P E J C I B B
FEB 0 1 2003
PATENT & TRADEMARK

O I P E J C I B B
FEB 0 3 2003
PATENT & TRADEMARK

Substitute PTO/SB/8A (08-00)

Approved for use through 10/31/2002. OMB 0651-0031

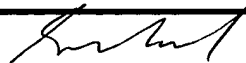
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for PTO/SB/8A (08-00) (Modified)			Complete if Known		
			Application Number	09/990,433	
			Filing Date	November 20, 2001	
			First Named Inventor	ZARLING, David A.	
			Group Art Unit	4633-1636	
			Examiner Name	KAUSHAL	
Sheet	6	of	8	Attorney Docket Number	A-64580-5/RFT/NBC (467135-38)

RECEIVED
FEB 03 2003
TECH CENTER 1600/25

OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	7*
SL	C53	MULLER, et al., "RecA-mediated annealing of single-stranded DNA and its relation to the mechanism of homologous recombination," J. Mol. Biol., 221:131-145 (1991).	
SL	C54	MULLINS, J.J., et al., "Expression of the DBA/2J Ren-2 gene in the adrenal gland of transgenic mice." EMBO J. 1989 Dec 20;8(13):4065-72	
SL	C55	MULLINS, J.J. et al., "Fulminant hypertension in transgenic rats harbouring the mouse Ren-2 gene." Nature. 1990 Apr 5;344(6266):541-4	
SL	C56	O'GORMAN, et al., "Recombinase-mediated gene activation and site-specific integration in mammalian cells," Science, 251:1351-1355 (1991).	
SL	C57	ORKIN et al., "Report and Recommendations of the Panel to Assess the NIH Investment in Research on Gene Therapy," National Institutes of Health, 7 December 1995.	
SL	C58	WAPATI, W., et al., "Sequence-Specific DNA Targeting", Encyclo. of Cancer, Vol. III:1601-1625 (1997).	
SL	C59	PENNISI, "The Lamb That Roared," Science 278:2038-2039 (1997).	
SL	C60	PENNISI, "After Dolly, a Pharming Frenzy," Science 279:646-648 (1998).	
SL	C61	PLATENBURG, et al., "Mammary-gland-specific hypomethylation of Hpa II Sites Flanking the Bovine α -S1-Casein gene," Transgenic Research, 5:421-431 (1996).	
SL	C62	PODYMINOGIN, M.A., et al., "RecA-Catalyzed, Sequence-Specific Alkylation of DNA by Cross-Linking Oligonucleotides. Effects of Length and Nonhomologous Base Substitutions", Biochemistry, 35:7267-7274 (1996).	
SL	C63	PODYMINOGIN, M.A., et al., "Sequence-Specific Covalent Modification of DNA by Cross-Linking Oligonucleotides. Catalysis by RecA and Implication for the Mechanism of Synaptic Joint Formation", Biochemistry, 34:13098-13108 (1995).	
SL	C64	PRELLE, et al., "Beneficial Effects of Thiol Compounds on Hatching Rate and ICM Outgrowth of Bovine IVM/IVF Embryos," Biol. Reprod. 54(51):172 [No. 463] (1996).	
SL	C65	RASHID, N., et al., "Characterization of a RecA/RAD51 homologue from the hyperthermophilic archaeon Pyrococcus sp. KOD1", Nucleic Acids Research, Vol. 25, No.4:719-726 (1997).	
SL	C66	RAWLS, R., "Hybrid DNA-RNA efficiently repairs gene", C&EN, p.11 (Sep. 1996).	
SL	C67	REISS, B., et al., "RecA protein stimulates homologous recombination in plants", Proc. Natl. Acad. Sci. USA, 93:3094-3098 (Apr. 1996).	
SL	C68	RENET, B.M.J., et al., "Homologous DNA Targeting with RecA Protein-coated Short DNA Probes and Electron Microscope Mapping on Linear Duplex Molecules", rep. fr. J. Mol. Biol., 232:779-791 (1993).	

Examiner Signature		Date Considered	10/6/03
--------------------	---	-----------------	---------

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Unique citation designation number. ² See attached Kinds of U.S. Patent Documents at www.uspto.gov or MPEP 901.04. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶ Applicant is to place a check mark here if English Language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231. 1102232_1.DOC

FEB 01 2003

FEB 03 2003

Substitute PTO/SB/8A (08-00)

Approved for use through 10/31/2002. OMB 0651-0031

U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449A/PTO
(Modified)**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

(use as many sheets as necessary)

Sheet

7

of

8

Complete if Known

Application Number	09/990,433
Filing Date	November 20, 2001
First Named Inventor	ZARLING, David A.
Group Art Unit	1633 / 636
Examiner Name	KAUSHAL
Attorney Docket Number	A-64580-5/RFT/NBC (467135-38)

RECEIVED

FEB 03 2003

TECH CENTER 1600/23

OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	†
SC	C69	ROMAGNOLO, et al., "Regulation of expression of IGF-I-induced IGFBP-3 and IGF-I-receptor by constitutive vs regulated expression of recombinant IGF-I in transfected mammary epithelial cells," Endocrine Journal 2:375-384 (1994).	
SC	C70	SABURI, et al., "Production and Analysis of Germ Line Chimeras Derived from a Single ES Cell Microinjected into 8-Cell Stage Embryo of the Mouse," Biol. Reprod. 54(51):172 [464] (1996).	
SC	C71	SAUER and HENDERSON, "Targeted Insertion of Exogenous DNA into the Eukaryotic Genome by the Cre Recombinase," New Biologist, 2:441-449 (1990).	
SC	C72	SCHNIEKE, et al., "Human Factor IX Transgenic Sheep Produced by Transfer of Nuclei from Transfected Fetal Fibroblasts," Science 278:2130-2133 (1997).	
SC	C73	SENA, E.P., et al., "Targeting in linear DNA duplexes with two complementary probe strands for hybrid stability," Nature Genetics, 3:365-372 (Apr. 1993).	
SC	C74	SHANER et al., "The distribution of Escherichia coli recA protein bound to duplex DNA with single-stranded ends," Journal of Biological Chemistry, 262(19):9220-9230 (1987).	
SC	C75	SHIBATA, et al., "Homologous pairing in genetic recombination: Complexes of recA protein and DNA," Proc. Natl. Acad. Sci. USA, 76(10):5100-5104 (1979).	
SC	C76	SHINKEL, T.A. et al., "Changes in cell surface glycosylation in alpha1,3-galactosyltransferase knockout and alpha1,2-fucosyltransferase transgenic mice." Transplantation. 1997 Jul 27;64(2):197-204	
SC	C77	SMITHIES et al., "Insertion of DNA Sequences into the Human Chromosomal -Globin Locus by Homologous Recombination," Nature, 317:230-234 (1985).	
SC	C78	SOLTIS, et al., "RecA protein promoted DNA strand exchange," The Journal of Biological Chemistry, 258(10):6073-6077 (1983).	
SC	C79	STEMMER, W.P.C., et al., "Single-step assembly of a gene and entire plasmid from large numbers of oligodeoxyribonucleotides," Gene, 164:49-53 (1995).	
SC	C80	STEMMER, W.P.C., "DNA shuffling by random fragmentation and reassembly: In vitro recombination for molecular evolution," Proc. Natl. Acad. Sci. USA, Vol. 91:10747-10751 (Oct. 1994).	
SC	C81	STEMMER, W.P.C., "Rapid evolution of a protein in vitro by DNA shuffling," Nature, 370:389-391 (Aug. 1994).	
SC	C82	STICE, et al., "Pluripotent Bovine Embryonic Cell Lines Direct Embryonic Development Following nuclear Transfer," Biology of Reproduction, 54:100-110 (1996).	
SC	C83	STICE, et al., "Multiple Generational Bovine Embryo Cloning," Biol. Reprod. 48:715-719 (1993).	
SC	C84	TABONE, J.C. et al., "Factors Influencing the Extent and Regiospecificity of Cross-Link Formation between Single-Stranded DNA and Reactive Complementary Oligodeoxynucleotides," Biochemistry, 33(1):375-383 (1994).	

Examiner
SignatureDate
Considered

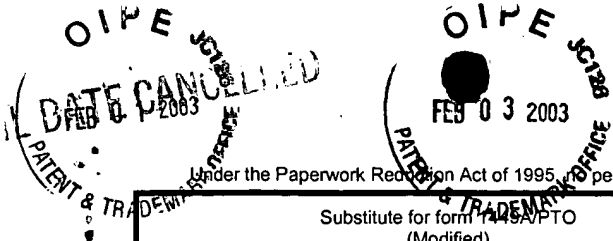
10/6/03

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Unique citation designation number. ² See attached Kinds of U.S. Patent Documents at www.uspto.gov or MPEP 901.04. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible.

⁶ Applicant is to place a check mark here if English Language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231. 1102232_1.DOC



Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form PTO/SB/PTO (Modified) INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary)			Complete if Known		
			Application Number	09/990,433	
			Filing Date	November 20, 2001	
			First Named Inventor	ZARLING, David A.	
			Group Art Unit	1633 KAUSHALE 1636	
			Examiner Name	KAUSHALE	
Sheet	8	of	8	Attorney Docket Number	A-64580-5/RFT/NBC (467135-38)

OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS		
Examiner Initials*	Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.
✓	C85	TAUROG, J.D., et al., "HLA-B27 in inbred and non-inbred transgenic mice. Cell surface expression and recognition as an alloantigen in the absence of human beta 2-microglobulin." J Immunol. 1988 Dec 1;141(11):4020-3
✓	C86	THOMAS et al., "High Frequency Targeting of Genes to Specific Sites in the Mammalian Genome," Cell, 44:419-428 (1986).
✓	C87	TOMAN, et al., "Production of Recombinant Human Type I Procollagen in the Mammary Gland of Transgenic Mice," Collagen Corporation 1-19 (5 FIG. Sheets).
✓	C88	TOUCHETTE, Nat. Med. 2(1)7-8 (Jan. 1996)
✓	C89	TURNER, et al., "Role of Tissue Remodeling in Mammary Epithelial Cell Proliferation and Morphogenesis," J. Dairy Sci. 74:2801-2807 (1991).
✓	C90	VALANCIUS and SMITHIES, "Testing and "In-Out" Targeting Procedure for Making Subtle Genomic Modifications in Mouse Embryonic Stem Cells," Molecular and Cellular Biology, 11(3):1402-1408 (1991).
✓	C91	VERMA, I.M. and Somia, N. "Gene therapy — promises, problems and prospects." Nature. 1997 Sep 18;389(6648):239-42.
✓	C92	VOLOSHIN, O.N., et al., "Homologous DNA pairing promoted by a 20 amino acid peptide derived from RecA", Science, 272:868-872 (1996).
✓	C93	WALL, R.J., "Transgenic livestock: Progress and prospects for the future." Theriogenology 45:57-68 (1996)
✓	C94	WOO, J., et al., "G/C-modified oligodeoxynucleotides with selective complementarity: synthesis and hybridization properties", Nucleic Acids Res., 24(13):2470-2475 (1996).
✓	C95	WOODWARD, et al., "Inhibition of Cellular Proliferation and Modulation of Insulin-Like Growth Factor Binding Proteins by Retinoids in a Bovine Mammary Epithelial Cell Line," Journal of Cellular Physiology, 167:488-499 (1996).
✓	C96	WU et al., "Targeting Genes: Delivery and Persistent Expression of a Foreign Gene Driven by Mammalian Regulatory Elements in Vivo," The Journal of Biological Chemistry, 264(29):16985-16987 (1989).
✓	C97	YOON, K., et al., "Targeted gene correction of episomal DNA in mammalian cells mediated by a chimeric RNA-DNA oligonucleotide", Proc. Natl. Acad. Sci. USA, 93:2071-2076 (Mar. 1996).
✓	C98	ZILINSKAS, "Bioethics and Biological Weapons," Science 279:635 (1998).
✓	C99	"Production of Recombinant Proteins in the Milk of Transgenic Animals," Genzyme Transgenics 3-30.
	C100	
	C101	
	C102	

Examiner Signature		Date Considered	10/6/03
--------------------	--	-----------------	---------

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Unique citation designation number. ² See attached Kinds of U.S. Patent Documents at www.uspto.gov or MPEP 901.04. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶ Applicant is to place a check mark here if English Language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231. 1102232_1.DOC